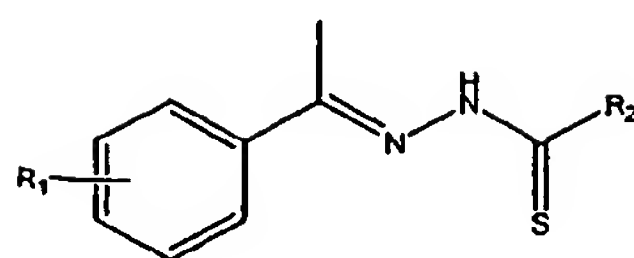
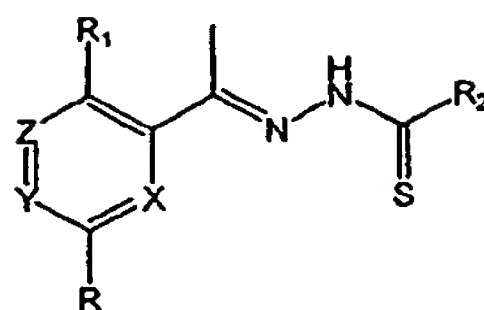


FIG. 1



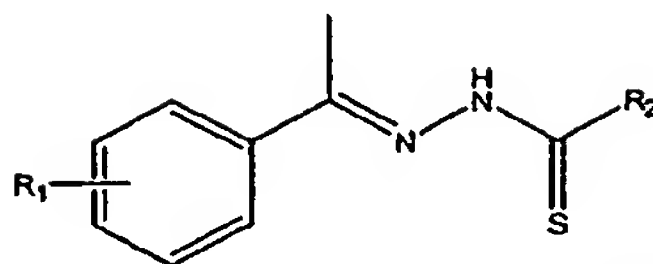
Cmpd#	R1	R2	Cruzain IC50 (μ M)	<i>T. cruzi</i> Survival (days @ 5 μ M)	Host Toxicity
1a	2'-phenyl	NH ₂	>20	5 days	none
1b	3'-phenyl	NH ₂	8	43 days	none
1c	4'-phenyl	NH ₂	5	8 days	toxic
2a	2'-NH-phenyl	NH ₂	>20	5 days	none
2b	3'-NH-phenyl	NH ₂	>20	43 days	none
2c	4'-NH-phenyl	NH ₂	>20	43 days	none
2d	3'-O-phenyl	NH ₂	10	27 days	toxic
2e	4'-O-phenyl	NH ₂	10	28 days	toxic
3d	3'-Br	NH ₂	0.06	43 days	none
3e	3'NH ₂	NH ₂	>20	5 days	none
3f	2'-OH	NH ₂	>20	5 days	none
3g	3'-OH	NH ₂	>20	5 days	none
3h	4'-OH	SMe	>20	5 days	none
4a	3'-Br	Shit	>20	7 days	toxic
4c	3'-Br	piperidyl	5	5 days	none
4d	3'-Br	N-methylpiperazinyl	5	14 days	toxic
4e	3'-Br	NEt ₂	5	5 days	none

FIG. 2



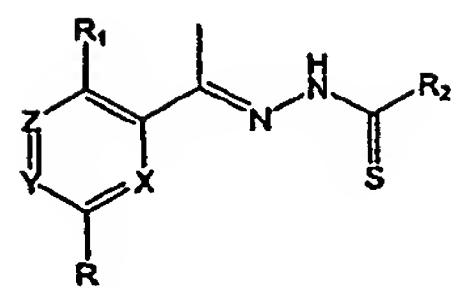
Cmpd#	R	R1	R2	X	Y	Z	Cruzain IC50(μ M)	<i>T. cruzi</i> Survival (days @5 μ M)	Host Toxicity
3a	H	H	NH ₂	N	CH	CH	>20	43 days	none
3b	H	H	NH ₂	CH	N	CH	>20	5 days	none
3c	H	H	NH ₂	CH	CH	N	>20	5 days	none
4b	H	H	SMe	N	CH	CH	>20	5 days	none
3i	CH(Me)NNHC(S)NH ₂	H	NH ₂	CH	CH	CH	5	5 days	none
3j	CH(Me)NNHC(S)NH ₂	H	NH ₂	N	CH	CH	>20	5 days	none
3k	CH(Me)NNHC(S)NH ₂	Me	NH ₂	CH	CMe	N	>20	5 days	none

FIG. 3



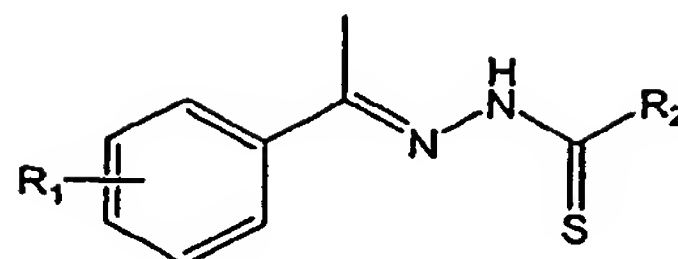
Cmpd#	R1	R2	Rhodesain IC50(μ M)	<i>T. brucei</i> ED50 (μ M)
1a	2'-phenyl	NH ₂	>20	>20
1b	3'-phenyl	NH ₂	1.1	12
1c	4'-phenyl	NH ₂	0.09	10
2a	2'-NH-phenyl	NH ₂	>20	>20
2b	3'-NH-phenyl	NH ₂	0.8	8
2c	4'-NH-phenyl	NH ₂	18	4.5
2d	3'-O-phenyl	NH ₂	0.55	6
2e	4'-O-phenyl	NH ₂	8	3
3d	3'-Br	NH ₂	0.05	>20
3e	3'-NH ₂	NH ₂	>20	>20
3f	2'-OH	NH ₂	>20	>20
3g	3'-OH	NH ₂	>20	>20
3h	4'-OH	NH ₂	>20	>20
4a	3'-Br	SMe	>20	10
4c	3'-Br	piperidyl	4	3
4d	3'-Br	N-methylpiperaziny	4	2
4e	3'-Br	NEt ₂	1.8	3

FIG. 4



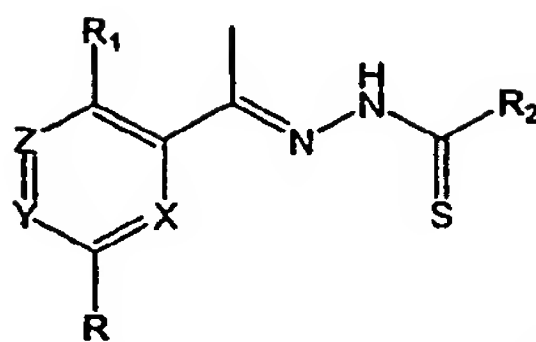
Cmpd#	R	R1	R2	X	Y	Z	Rhodesain	T.brucei
							IC50(μM)	ED50(μM)
3a	H	H	NH ₂	N	CH	CH	>20	4
3b	H	H	NH ₂	CH	N	CH	>20	>20
3c	H	H	NH ₂	CH	CH	N	>20	>20
4b	H	H	SMe	N	CH	CH	>20	0.3
3i	CH(Me)NNHC(S)	H	NH ₂	CH	CH	CH	0.33	>20
3j	CH(Me)NNHC(S)	H	NH ₂	N	CH	CH	>20	>20
3k	CH(Me)NNHC(S) NH ₂	Me	NH ₂	CH	CMe	N	>20	>20

FIG. 5



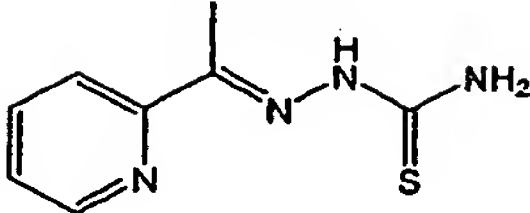
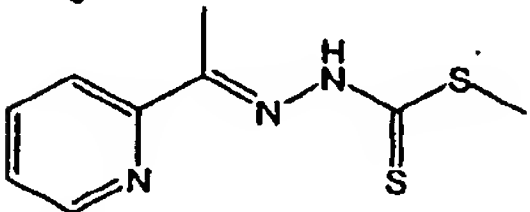
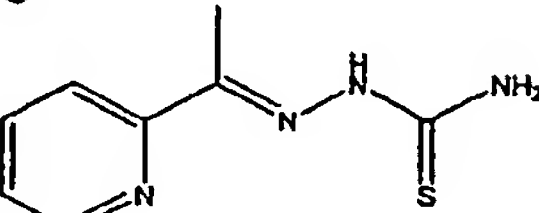
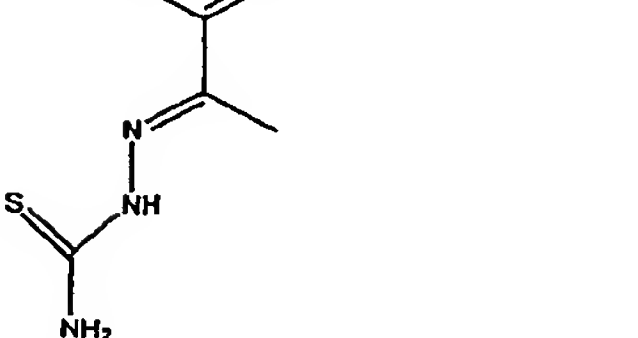
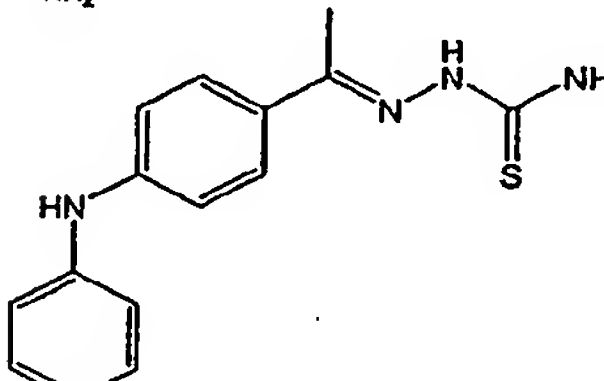
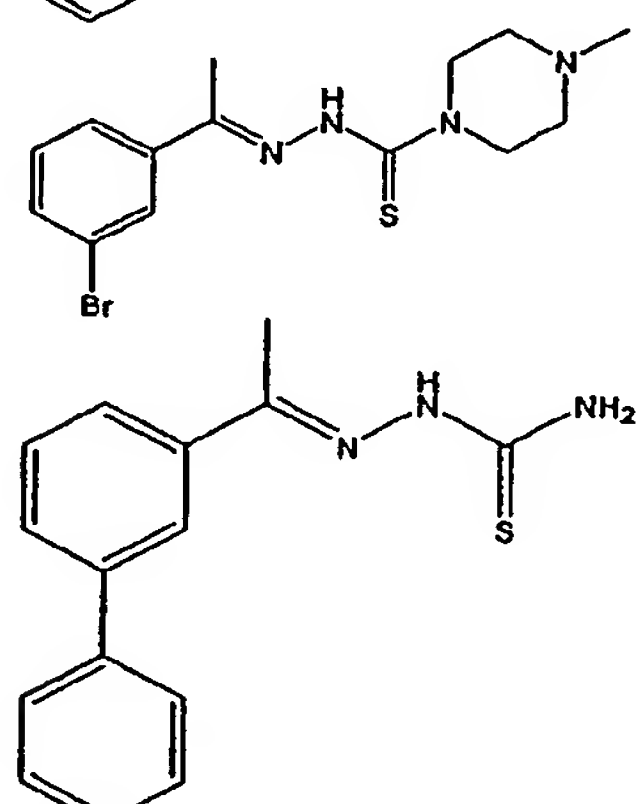
Cmpd#	R1	R2	Falcipain 2 IC50(μM)	<i>P.falciparum</i> ED50(μM)
1a	2'-phenyl	NH ₂	>20	>20
1b	3'-phenyl	NH ₂	>20	>20
1c	4'-phenyl	NH ₂	10	>20
2a	2'-NH-phenyl	NH ₂	>20	>20
2b	3'-NH-phenyl	NH ₂	>20	>20
2c	4'-NH-phenyl	NH ₂	>20	9.9
2d	3'-O-phenyl	NH ₂	>20	>20
2e	4'-O-phenyl	NH ₂	>20	>20
3d	3'-Br	NH ₂	>20	>20
3e	3'-NM ₂	NH ₂	>20	>20
3f	2'-OH	NH ₂	>20	>20
3g	3'-OH	NH ₂	>20	>20
3h	4'-OH	NH ₂	>20	>20
4a	3'-Br	SMe	>20	>20
4c	3'-Br	piperidyl	>20	20
4d	3'-Br	N-methylpiperazinyl	>20	4
4e	3'-Br	NEt ₂	>20	>20

FIG. 6



Cmpd#	R	R1	R2	X	Y	Z	Falcipain 2 IC50(μm)	P. falciparum ED50(μm)
3a	H	H	NH ₂	N	CH	CH	>20	0.08
3b	H	H	NH ₂	CHN	CH	CH	>20	>20
3c	H	H	NH ₂	CHCH	N	CH	>20	>20
4b	H	H	SMe	N	CH	CH	>20	0.03
3i	CH(Me)NNHC(S)NH ₂	H	NH ₂	CHCH	CH	CH	>20	>20
3j	CH(Me)NNHC(S)NH ₂	K	NH ₂	N	CH	CH	>20	0.03
3k	CH(Me)NNHC(S)NH ₂	Me	NH ₂	CHCMe	N	CH	>20	>20

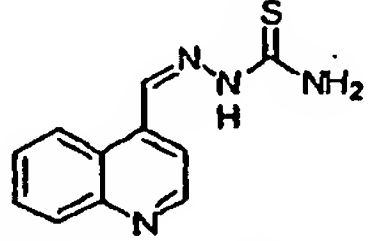
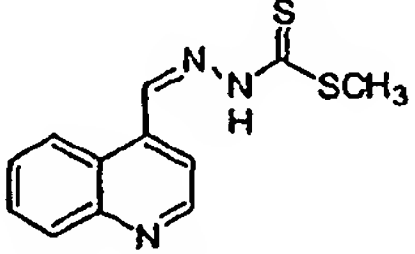
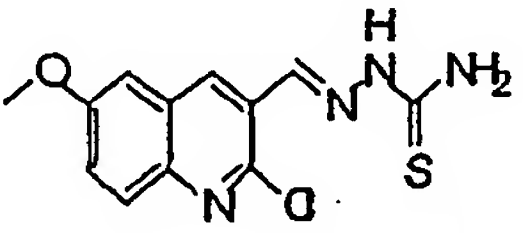
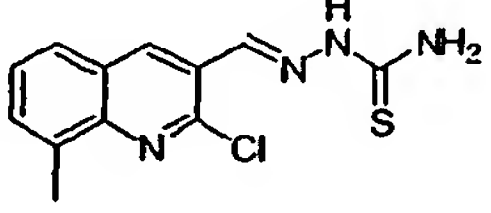
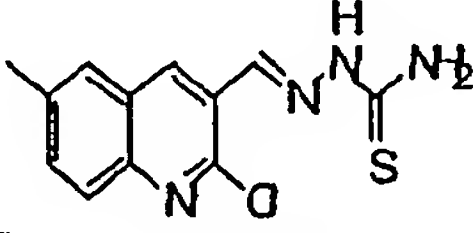
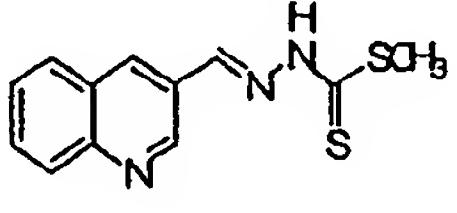
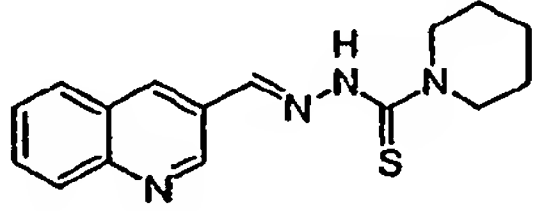
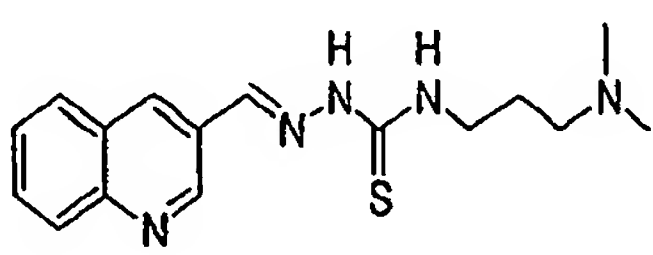
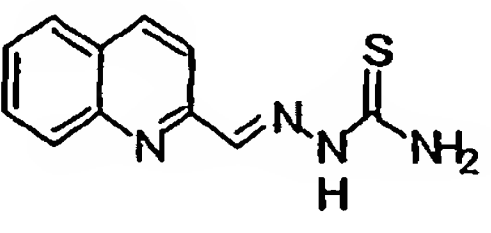
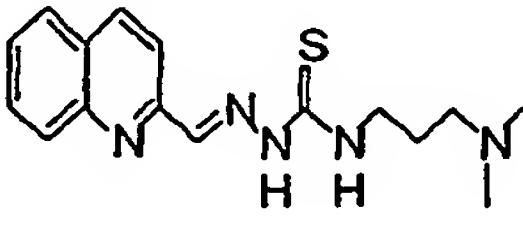
FIG. 7

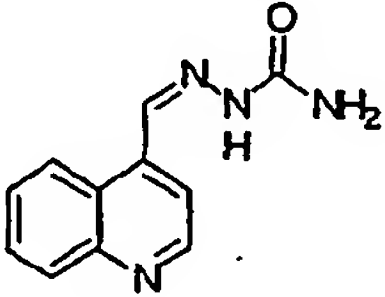
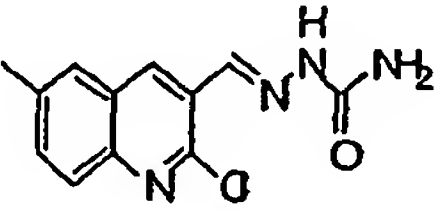
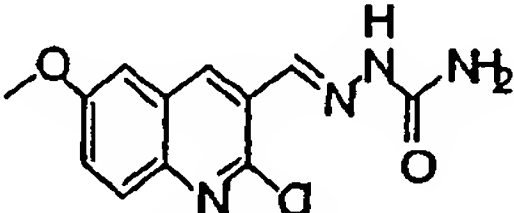
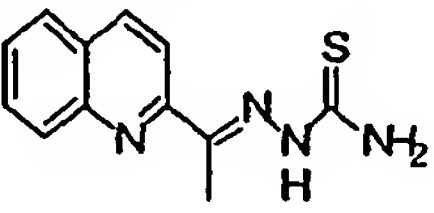
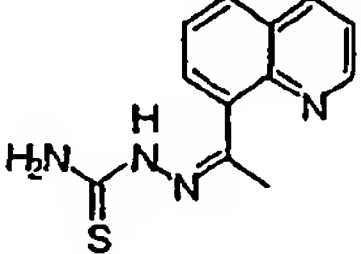
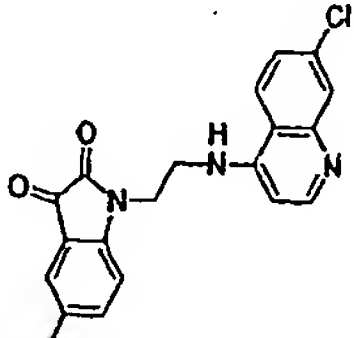
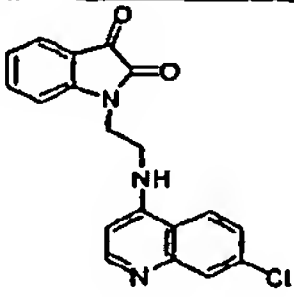
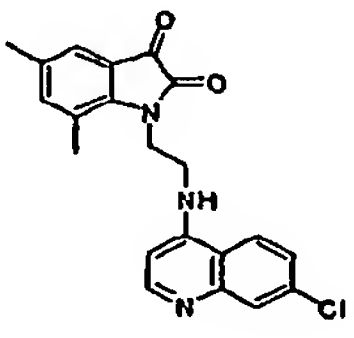
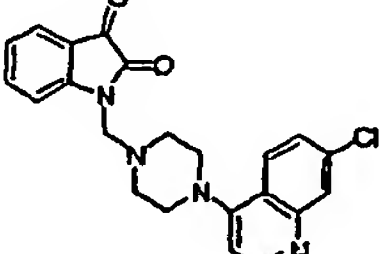
Compound	Structure	Survival (toxicity)	
		5 mgs/kg weight	20mgs/kg weight
3a		20 hours (*)	62 hours (**)
4b		62 hours (No)	62 hours (No)
3j		62 hours (No)	62 hours (No)
2c		62 hours (No)	62 hours (No)
4d		62 hours (No)	62 hours (No)
1b		62 hours (No)	62 hours (No)

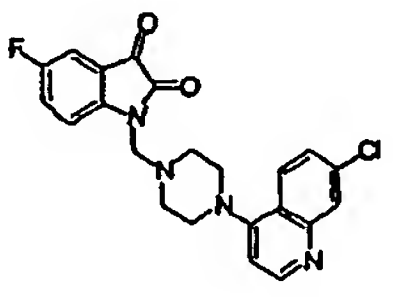
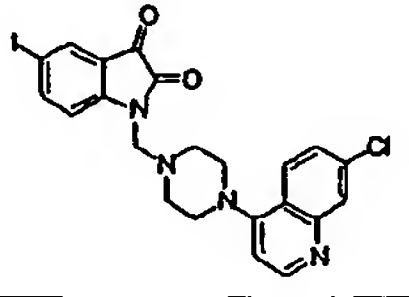
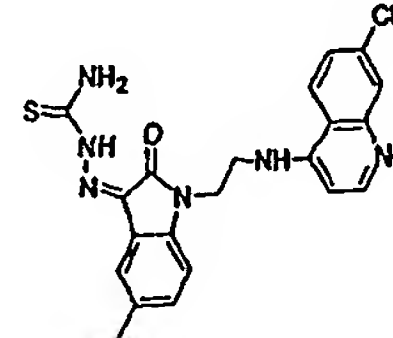
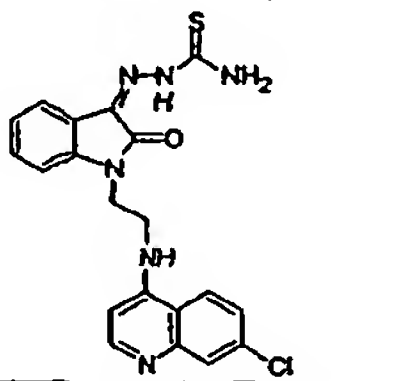
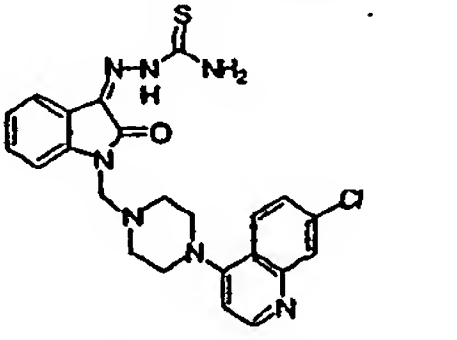
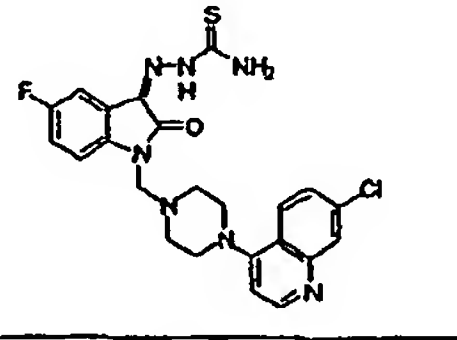
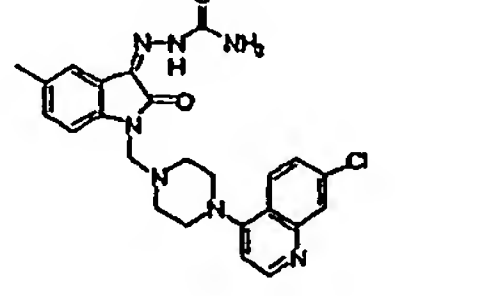
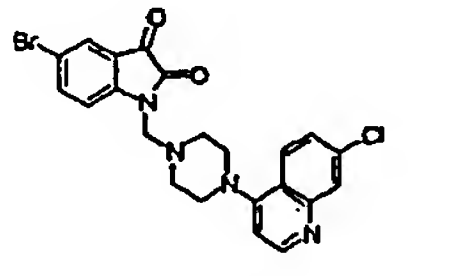
*Animal suffered toxic shock after injection, characterization by tremor, loss of mobility, malaise, and death

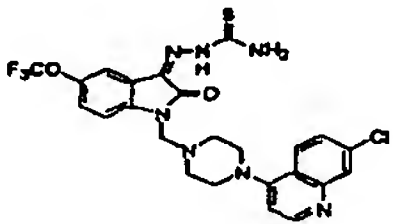
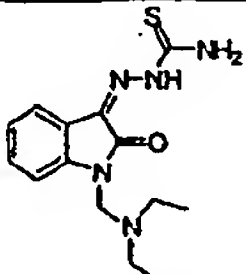
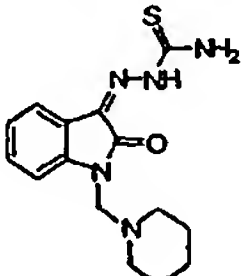
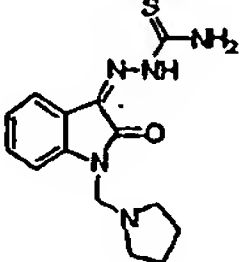
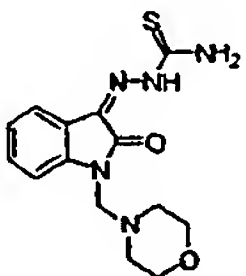
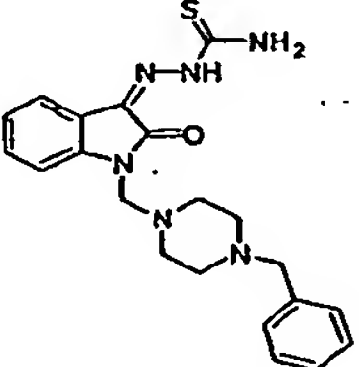
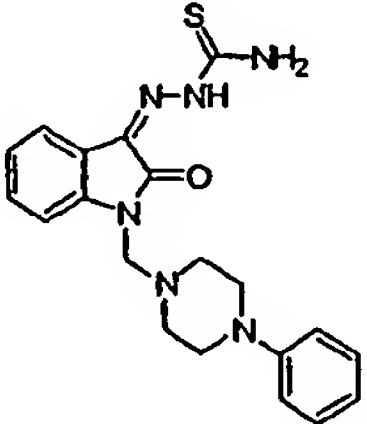
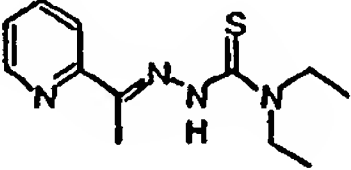
**Animal survived treatment with malaise, loss of mobility and ruffled hair after injection

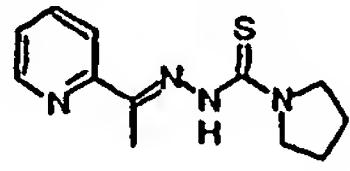
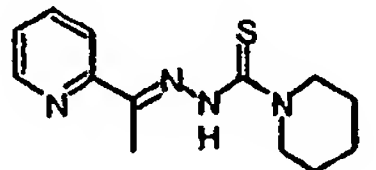
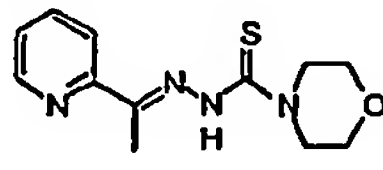
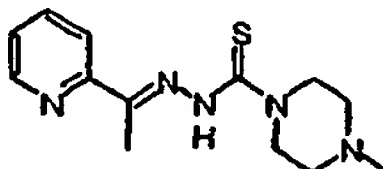
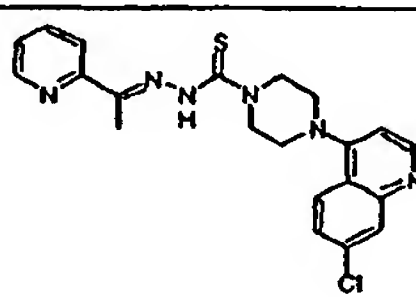
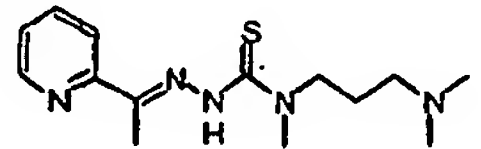
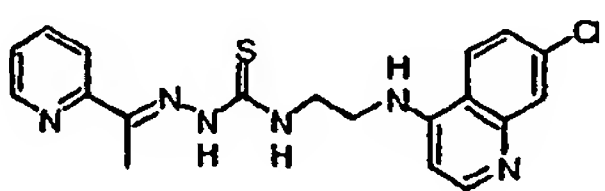
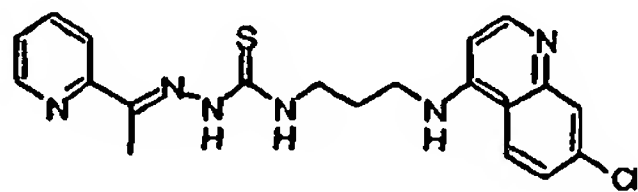
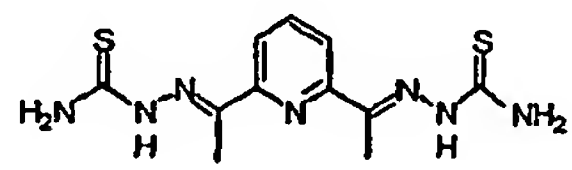
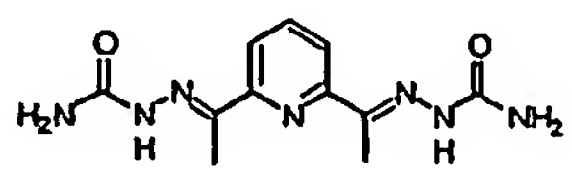
FIG. 8

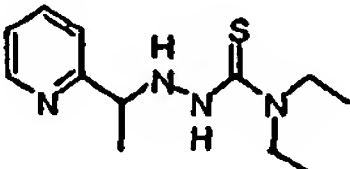
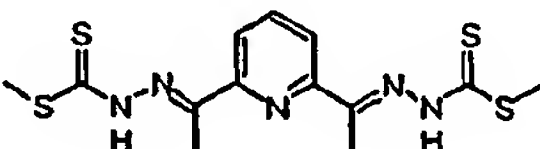
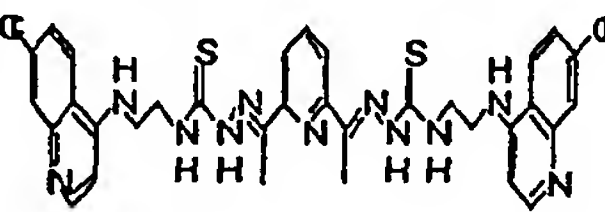
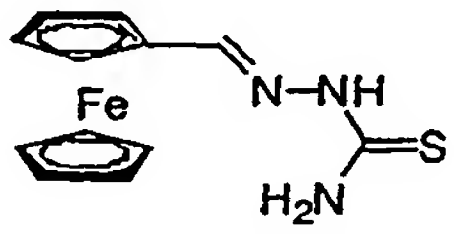
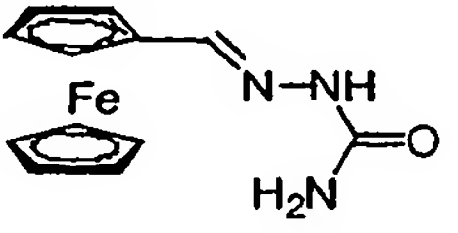
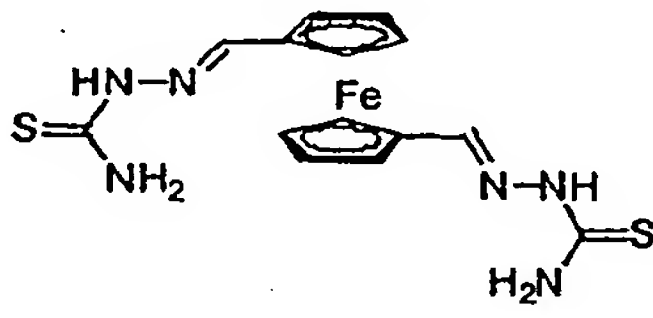
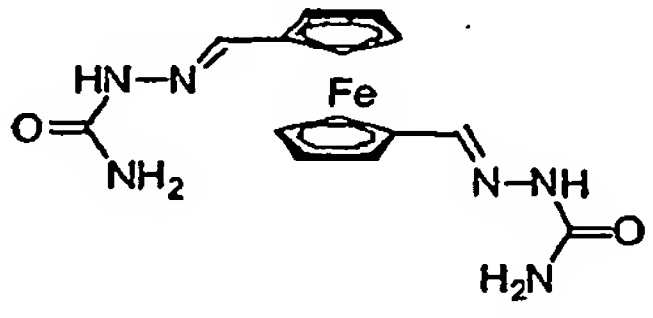
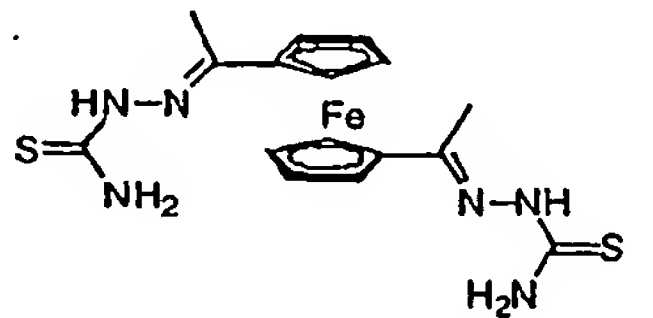
Structure	Cruzain IC ₅₀ (μ M)	Rhodesain IC ₅₀ (μ M)	P. falciparum W2 IC ₅₀ (μ M)
	1.5	0.4	>20
	>10	>10	>20
	>10	9	>20
	0.312	5	>20
	>10	not determined (ND)	>20
	>10	>10	>20
	>10	>10	>20
	>10	>10	3.3
	>10	5	>20
	>10	>10	7.7

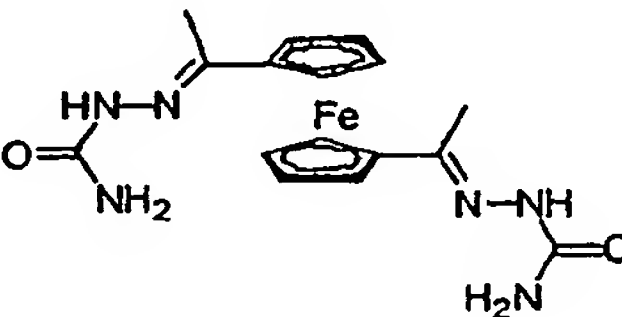
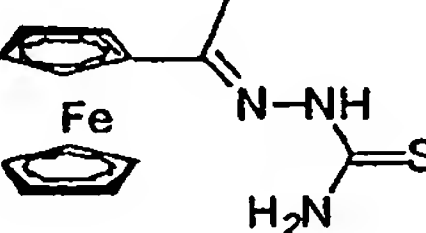
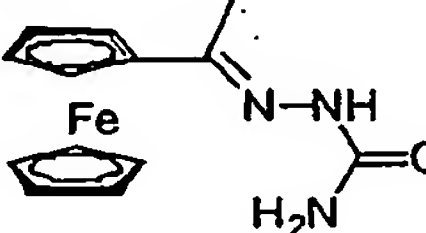
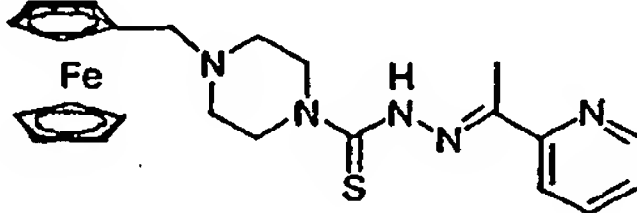
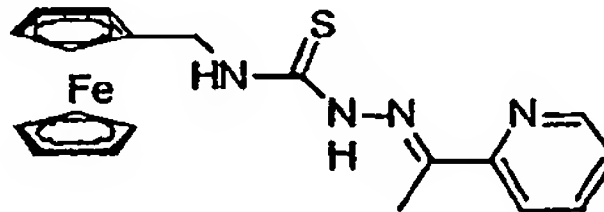
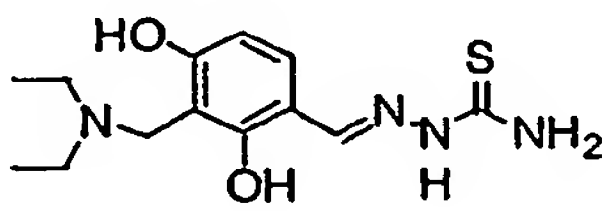
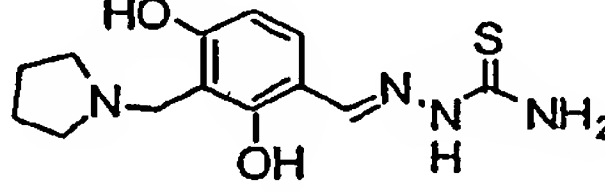
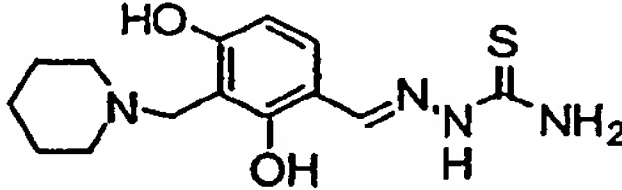
Structure	Cruzain IC ₅₀ (μ M)	Rhodesain IC ₅₀ . (μ M)	P. falciparum W2 IC ₅₀ (μ M)
	>10	>10	>20
	>10	>10	>20
	>10	>10	>20
	5	0.8	2.5
	>10	ND	>20
	>10	>10	0.489
	>10	>10	0.125
	>10	>10	0.227
	>10	>10	0.961

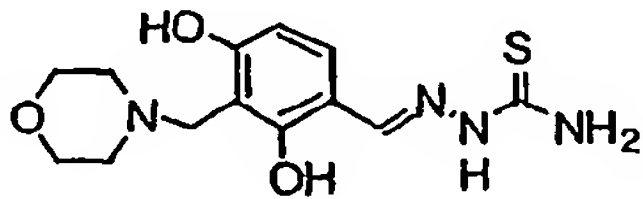
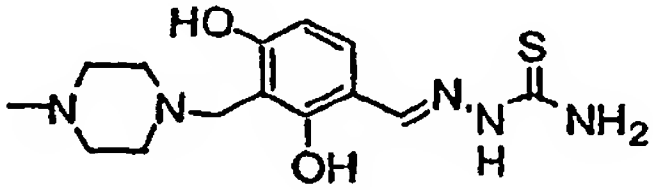
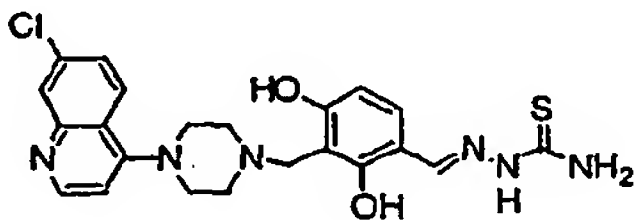
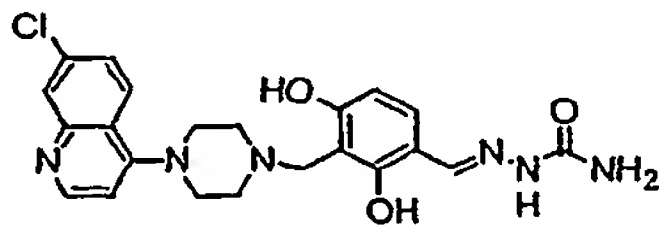
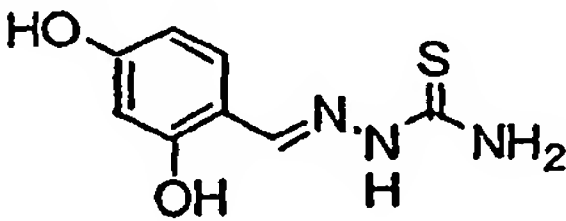
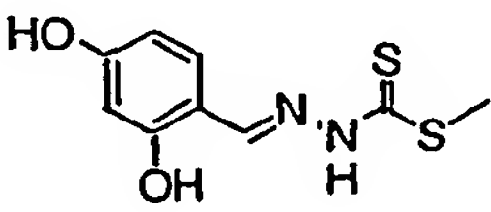
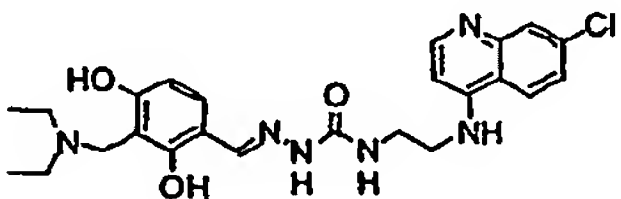
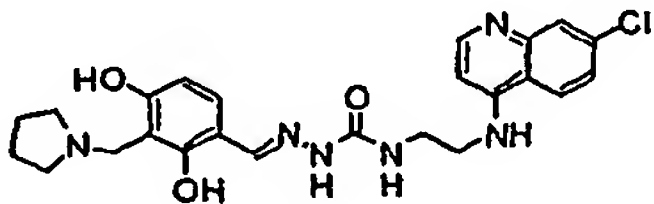
Structure	Cruzain IC50 (μ M)	Rhodesain IC50 (μ M)	P. falciparum W2 IC50 (μ M)
	>10	>10	0.908
	>10	>10	0.794
	2	4	0.051
	ND	ND	0.242
	>10	8	0.957
	ND	4	1.193
	ND	3	1.809
	ND	1	1.226

Structure	Cruzain IC50 (μ M)	Rhodesain IC50 (μ M)	P. falciparum W2 IC50 (μ M)
	ND	5	0.833
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	4	0.025

Structure	Cruzain IC ₅₀ (μ M)	Rhodesain IC ₅₀ (μ M)	P. falciparum W2 IC ₅₀ (μ M)
	1.8	0.11	0.008
	1.6	4	0.028
	ND	ND	0.013
	ND	0.7	0.013
	ND	ND	0.212
	ND	1.8	0.26
	ND	0.42	0.212
	ND	ND	0.19
	ND	4	6.521
	ND	5.5	0.14

Structure	Cruzain IC ₅₀ (μ M)	Rhodesain IC ₅₀ (μ M)	P. falciparum W2 IC ₅₀ (μ M)
	>10	ND	0.032
	1.5	0.3	1.677
	0.8	0.4	0.054
	8.5	ND	>20
	ND	ND	>20
	3.5	4.2	>20
	ND	ND	>20
	2	1.8	>20

Structure	Cruzain IC50 (μ M)	Rhodesain IC50 (μ M)	P. falciparum W2 IC50 (μ M)
	ND	ND	>20
	>10	10	>20
	ND	ND	>20
	ND	ND	0.0246
	ND	ND	0.0161
	9	4	>20
	2.1	2	>20
	5	3	>20

Structure	Cruzain IC ₅₀ (μ M)	Rhodesain IC ₅₀ (μ M)	P. falciparum W2 IC ₅₀ (μ M)
	20	10	>20
	ND	7	>20
	ND	1	0.376
	ND	>10	0.246
	ND	ND	>20
	ND	ND	>20
	ND	5	0.437
	2.8	2.5	1.065

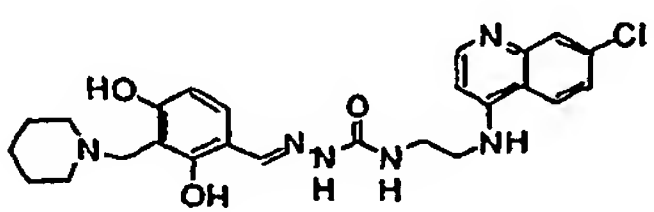
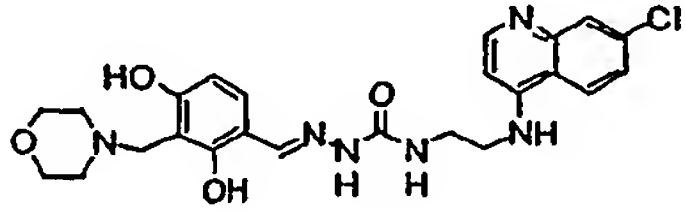
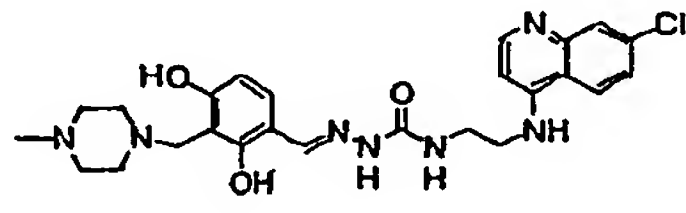
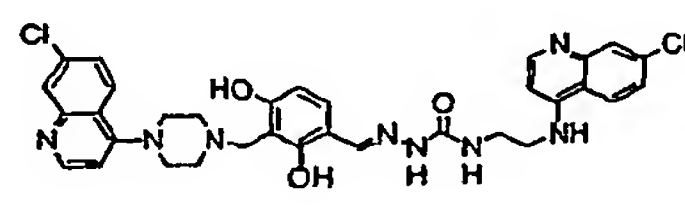
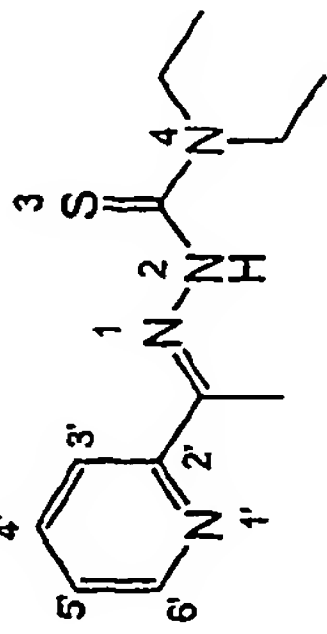
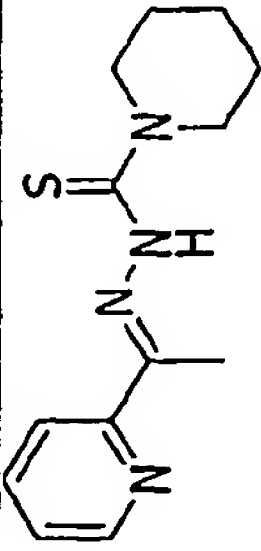
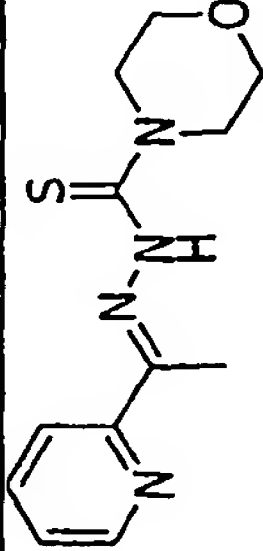
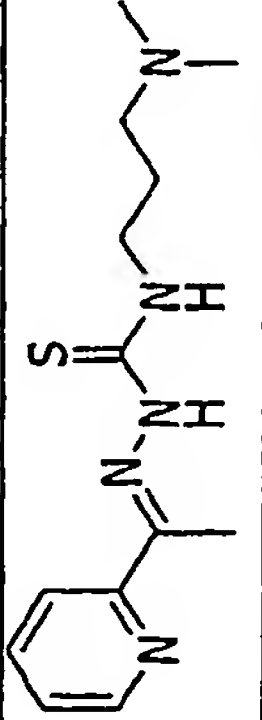
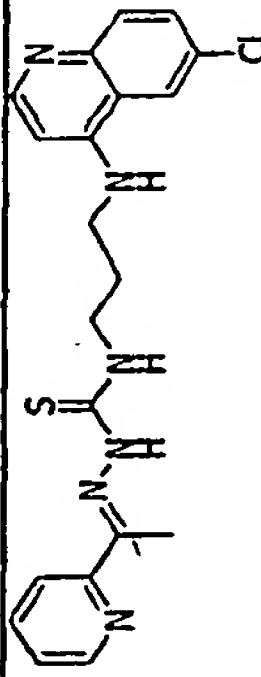
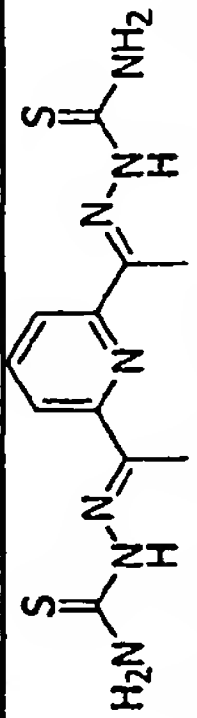
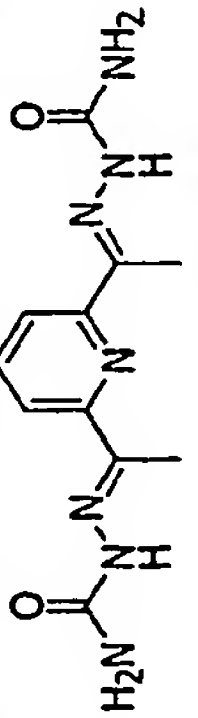
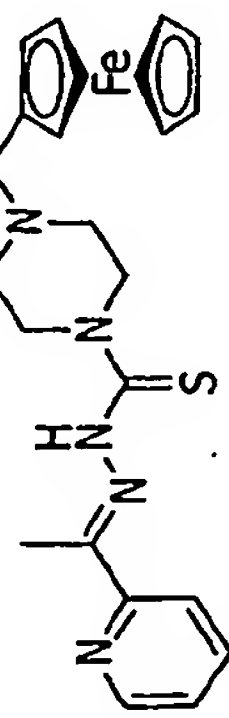
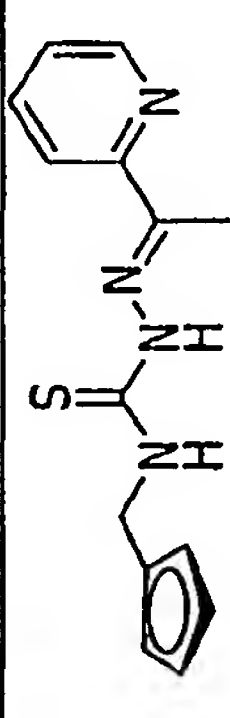
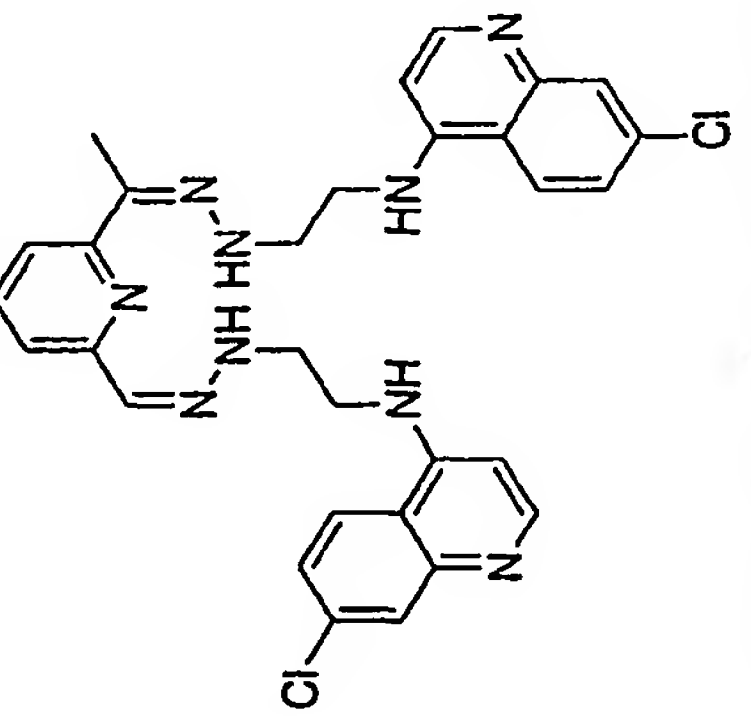
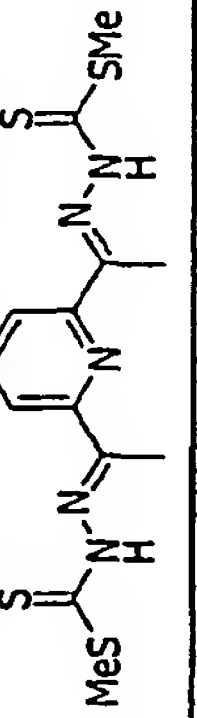
Structure	Cruzain IC50 (μ M)	Rhodesain IC50 (μ M)	<i>P. falciparum</i> W2 IC50 (μ M)
	1.8	1.8	0.265
	>10	>10	0.113
	ND	ND	0.376
	3.5	ND	0.077

FIG. 9

Compound Structure	Compound ID	30	% inhibition T. brucei		1	ED ₅₀ µg/ml	repeat	Cytotoxicity ED ₅₀ µg/ml	Therapeutic Index
			10	3		+/- 95% CL			
	MC 156	98.24	98.85	99.57	99.67	<1.11 @	0.0384 ± 0.0004	0.04	1
	MC 158	98.76	99.22	99.68	99.73	<1.11 @	0.0015 ± 0.0005	0.3	200
	MC 159	97.78	100	100	98.51	<1.11 @	0.265 ± 0.66	1.8	7
	MC 162	100	100	99.95	98.45	<1.11 @	0.0014 ± 0.0005	13.5	9643
	MC 164	99.72	99.54	99.52	99.39	<1.11 @	0.019 ± 0.009	10	526

Compound Structure	Compound ID	% inhibition T. brucei			ED ₅₀ µg/ml	repeat	Cytotoxicity		Therapeutic Index
		30	10	3			ED ₅₀ µg/ml	Index	
	MC 172	15.25	12.89	10.09	>30		>300	-	
	MC 172B	99.84	99.09	99.23	<1.11 @	0.552 ± 0.156	>300	-	
	MC 176	99.23	99.25	98.27	<1.11 @	1.331 ± 0.045	0.57	0	
	MC 177	100	99.87	99.92	<1.11 @	0.0537 ± 0.004	3.08	57	
	MC 184	97.82	98.31	98.46	<1.11 @	0.0009 ± 0.0005	18.2	20222	
	MC 186	99.44	99.76	99.74	<1.11 @	0.0182 ± 0.0012	2.9	159	